

WHAT IS CLAIMED IS:

1. A device for immobilizing biological material comprising a polymer substrate layer 20, 20', 20" having biological immobilizing properties preferably for protein or nucleic acid, the substrate layer deposited on a rigid support 12, and having an outer deposit-receiving region exposed to receive the biological material, wherein the substrate layer is ultra-thin, having a thickness t_{ut} less than about 5 micron.
2. The device of claim 1 wherein said substrate layer has binding properties for the biological material.
3. The device of claim 1 or 2 wherein the rigid support 12 defines a straight support surface e.g., a planar surface such as that of a microscope slide 10a or cylindrical surface, and said substrate layer 20, 20', 20" is a drawn coating applied directly or indirectly to the rigid support in the direction of said straight surface, preferably drawn substantially according to Fig. 14.
4. The device of any of the foregoing claims wherein the deposit-receiving region of said substrate layer 20, 20', 20" is in a surface-treated state for enhanced adhesion of deposits of biological material thereon, preferably the surface treatment being that provided by a corona treater 122.
5. The device of any of the foregoing claims, wherein at least one intervening layer 14, 14', 112 lies between said rigid support 12 and said ultra-thin polymer substrate layer 20, 20', 20", said intervening layer adherently joined on each of its oppositely directed faces to substance of said device.
6. The device of any of the claim 5, wherein immediately adjacent materials on opposite sides of a said intervening layer 14, 14', 112 are not as adhesively compatible with each other as each is with said intervening layer.

7. The device of claim 5 or 6, wherein said intervening layer 14, 14', 112 is an adherent oxide of metal, preferably an oxide of tantalum or aluminum, or a silica based material, e.g. colloidal silica or a soluble silicate such as sodium silicate.

8. The device of claim 5 or 6, wherein a said intervening layer 14, 14', 112 is of substance selected from the group consisting of silane, epoxy silane, polyisiline, PEI, GAP, an adherent metal oxide, colloidal silica and soluble silicates.

9. The device of claim 5 or 6, wherein a said rigid support 12 defines a straight support surface e.g., planar or cylindrical, and said intervening layer 14, 14', 112 is a drawn coating applied directly or indirectly to the rigid member in the direction of said straight surface, preferably drawn substantially according to Fig. 13, preferably said intervening layer 14, 14', 112 comprising colloidal silica or a soluble silicate.

10. The device of any of the foregoing claims wherein a surface of one of the constituents of said device, prior to being united with a next constituent layer of the device, is in a surface-treated state for enhanced adhesion of that surface to said next constituent layer.

11. The device of claim 5 or 6, wherein a said intervening layer 14, 14', 112 is at least partially opaque, the intervening layer blocking at least 30%, preferably blocking at least 50%, or often preferably blocking at least 70% of incident radiation at a wave length corresponding to the stimulating or emission wavelength of a fluorophore tag on biological material.

12. The device of claim 10, wherein the rigid support 12 has characteristic fluorescence or luminescence in response to incident stimulating radiation, a said intervening layer 14, 14', 112 being effective to at least substantially limit penetration of incident stimulating radiation from the substrate layer 20, 20', 20" to the support or limit penetration of fluorescent or luminescent radiation from the support to the substrate layer, or both.

13. The device of any of the claims 5-12 wherein a said intervening layer 14, 14', 112 is electrically conductive.

14. The device of claim 13 wherein an electric terminal is associated with said intermediate layer 14, 14', 112 for applying a voltage potential to or sensing the potential of said layer.

15. The device of claim 14 constructed and arranged such that electrical potential applied to said terminal is effective to provide a potential to the substrate layer 20, 20', 20" of the device, to promote binding or rejection of biological material exposed to said substrate layer.

16. The device of claim 5 or 6 constructed and arranged to support biological material for microscopy, wherein a said intervening layer 14, 14', 112 is an oxide of metal, preferably oxide of tantalum or aluminum, adapted to serve at least one of the functions of adhesively uniting, either directly or indirectly, said rigid support 12 with said deposit-receiving substrate layer 20, 20', 20", of providing an opaque barrier to prevent or substantially limit light passing between said deposit-receiving substrate layer 20, 20', 20" and said support 12, or of providing an electrically conductive layer as a means e.g. to electrically charge said substrate layer 20, 20', 20".

17. The device of any of the foregoing claims wherein the substrate layer 20, 20', 20" is adapted to receive a deposit of biological material 420 and to be temporarily engaged by an object adjacent the deposit, as by an elastomeric gasket 430, wherein the substrate layer is interrupted so that adherence of the substrate to the removed object does not disrupt the array, preferably an intervening adhesion promoting layer 14' beneath said substrate layer being interrupted such that a substrate layer 20" applied thereto is disrupted, for example by moat M, Fig. 23, 24, formed by a gap in a pattern of a metal oxide adhesion promoting intervening layer 14'.

18. The device of claim 17 in which said substrate layer is applied as a continuous fluid coating which separates on drying at interruptions of an adhesion promoting layer, such as the metal oxide layer.

19. The device of any of the foregoing claims constructed for use in microscopy, wherein an outer surface of the substrate layer 20, 20', 20" is constructed to receive deposits of biological material thereon in position exposed for direct illumination and inspection from the exterior.

5 20. The device of any of the claims 1-6, wherein the device is functionally at least partially transparent to pass effective light in at least one direction between a deposit on said substrate layer 20, 20', 20" and through said rigid support 12, for instance the device arranged to enable illumination of a deposit of biological material on said substrate layer 20, 20', 20" via said rigid support 12, or the device arranged to enable microscopic
10 inspection of a deposit of biological material on said substrate layer 20, 20', 20" via said rigid support 12, or the device arranged to enable microscopic inspection of a deposit of biological material on said substrate layer from both the exterior side of said substrate layer side and via the rigid support.

 21. A device for immobilizing biological material comprising a polymer substrate
15 layer 20, 20', 20" having biological immobilizing properties preferably for protein or nucleic acid, the substrate layer deposited on a rigid support 12, and having an outer deposit-receiving region exposed to receive biological material, wherein the rigid support defines a straight support surface e.g., planar or cylindrical, and said substrate layer is a drawn coating applied directly or indirectly to the rigid member in the direction of said
20 straight surface, preferably drawn substantially according to Fig. 14, preferably there being at least one intervening layer 14, 14', 112, which lies between said rigid support 12 and said ultra-thin polymer substrate layer 20, 20', 20", said intervening layer adherently joined on each of its oppositely directed faces to substance of said device and preferably wherein immediately adjacent materials on opposite sides of a said intervening layer 14,
25 14', 112 are not as adhesively compatible with each other as each is with said intervening layer.

 22. A device for immobilizing biological material comprising a polymer substrate layer 20, 20', 20" having biological immobilizing properties preferably for protein or nucleic acid, the substrate layer deposited on a rigid support 12, and having an outer
30 deposit-receiving region exposed to receive biological material, wherein at least one

intervening layer 14, 14', 112 lies between said rigid support and said polymer substrate layer, said intervening layer adherently joined to substance of said device on each of its oppositely directed faces and wherein a said intervening layer 14, 14', 112 is at least partially opaque to radiation employed to stimulate emission from the biological material, limiting or preventing transmission of radiation from said rigid support, preferably wherein immediately adjacent materials on opposite sides of a said intervening layer 14, 14', 112 are not as adhesively compatible with each other as each is with said intervening layer.

23. A device for immobilizing biological material comprising a polymer substrate layer 20, 20', 20" having biological immobilizing properties preferably for protein or nucleic acid, the substrate layer deposited on a rigid support 12, and having an outer deposit-receiving region exposed to receive biological material, wherein at least one intervening layer 14, 14', 112 lies between said rigid support and said polymer substrate layer, said intervening layer adherently joined to substance of said device on each of its oppositely directed faces, preferably immediately adjacent materials on opposite sides of a said intervening layer 14, 14', 112 are not as adhesively compatible with each other as each is with said intervening layer, and said intervening layer comprising an electrically conductive layer, for instance, wherein the electrically conductive layer is associated with at least one electrical terminal and the conductive layer and said electrical terminal are constructed and arranged to provide a potential to the receiving surface of said device to promote binding or rejection of material exposed to said outer deposit-receiving surface of said substrate layer.

24. The device of claims 21, 22 or 23 wherein one or more layers of said device is in a surface-treated state for enhanced adhesion to an overlying layer or for adhesion of deposits of biological material thereon.

25. A device for immobilizing biological material comprising a polymer substrate layer 20, 20', 20" having biological immobilizing properties preferably for protein or nucleic acid, the substrate layer deposited on a rigid support 12, and having an outer deposit-receiving region exposed to receive biological material, wherein the deposit-receiving region of said substrate layer is in a surface-treated state for enhanced adhesion

of deposits of biological material thereon, e.g. the surface treatment being that provided by a corona treater 122.

26. The device of any of the foregoing claims, wherein said substrate layer 20', 20" is substantially solid, preferably having a thickness less than about 5 micron, preferably less than 3, 2 or 1 micron and in preferred embodiments between about 0.1 and 0.5 micron.

27. The device of any of the foregoing claims 1-25, wherein said substrate layer 20, at least in its outer region, is micro-porous, preferably said substrate layer being micro-porous throughout its thickness, and preferably, said substrate layer having a thickness less than 3 micron, preferably less than 2 or 1 micron.

28. The device of any of the foregoing claims 1-27, wherein said substrate layer 20, 20', 20" is nitrocellulose or polystyrene, preferably residing on an intervening surface adhesion promoter layer 14, 14', 112, preferably that intervening layer comprising an adherent oxide of metal, preferably tantalum or aluminum oxide, or comprising colloidal silica or a soluble silicate that is preferably a drawn coating.

29. The device of any of the foregoing claims 1-27, wherein said substrate layer 20, 20', 20" is selected from the group consisting of nitrocellulose, polystyrene, cellulose acetate, cellulose triacetate, ethyl cellulose, activated nylon, polytetrafluoroethylene (PTFE), polyvinyl difluoride (PVDF), polyamide, polyvinylchloride (PVC), divinyl benzene, and agarose.

30. The device of claim 4, 10, 24 or 25 wherein said surface-treated state is the result of exposure of the respective surface to corona (see Fig. 12) or flame treatment, bombardment with charged particles including electrons, ions, and sub-atomic particles, or exposure to electromagnetic radiation, such as ultraviolet, gamma, or X-ray wavelengths.

31. The device of any of the foregoing claims, wherein said rigid support 12 is a microscope slide 10, preferably a frosted microscope slide (see Fig. 7A), preferably a

blank frosted glass slide, preferably said microscope slide coated with a metal oxide to which is adhered a drawn coating, as by the process shown in Fig. 13.

32. The device of any of the foregoing claims 1-30 in the form of a bio-cassette, a CD disk, the bottom of a multi-well plate, or a hollow tube.

5 33. The device of any of the claims 1-30 in the form of a multiwell plate 90 comprising an upper well-defining structure 94 and a bottom plate 95 comprising said substrate layer 20, 20', 20" and said upper well-defining structure and the upper surface of the bottom plate member being of dissimilar material, an adhesion promoting intervening layer being disposed between the upper well-defining structure and said bottom plate, the
10 well-defining structure being polystyrene or similar polymer and the support of said plate member being glass, fused quartz, silicon or ceramic, the adhesion promoting layer preferably comprising an adherent metal oxide, e.g., tantalum oxide or aluminum oxide, and preferably a layer of polystyrene or similar polymer being disposed over the adhesion promoting layer to which said well-defining structure is bonded.

15 34. The device of any of the foregoing claims including a localized reference deposit 420, Fig. 11 or Fig. 23 of stable fluorescent material, preferably characterized by a broad fluorescence spectrum, e.g. polyimide, and preferably disposed on said device in position to be read by an optical instrument such as a microscope or CCD sensor for quality control of production of the device, or as an intensity calibrator during reading of
20 fluorescence of substance deposited on said substrate layer 20, 20', 20".

35. The device of any of the foregoing claims, wherein said support 12 is selected from the group consisting of glass, fused quartz, silicon, plastic, PMMA or polystyrene, or for those claims not requiring transparency, of ceramic or a metal such as gold, aluminum or silver.

25 36. The device of any of the foregoing claims 1-35, wherein the outer surface of said substrate layer 20, 20', 20" is generally flat and arranged to receive the deposit of a spotted array of bio-material, see Figs. 11 or 13, or already carries an array of bio-material

spots either in unreacted state or in a reacted state as a result of performance of an assay in which at least some of the said spots carry a fluorescent label.

37. A method of forming the device of any of the foregoing claims including applying directly or indirectly to said rigid support a fluid containing said polymer of said
5 substrate layer under conditions to form said substrate layer, preferably by drawing the rigid support from a bath of coating composition.

38. The method of claim 37 including applying an adhesion-promoting layer directly or indirectly to said rigid support before application of said substrate layer, preferably by applying a metal, preferably tantalum or aluminum and allowing it to
10 oxidize, or applying soluble silica or colloidal silicate by drawing from a bath.

39. The method of claims 37 or 38 for devices produced with a solid film substrate layer, including maintaining forming conditions to produce a solid film coating as the substrate layer.

40. The method of claim 37 or 38 for devices produced with a micro-porous
15 substrate layer, including maintaining forming conditions to produce a micro-porous coating as the substrate layer.

41. The method of claim 39 or 40 including post-treating the substrate layer coating to alter its structure or properties, for instance subjecting the coating to corona discharge or to reactive gas or to structure-changing radiation, or to a combination of
20 solvents selected to form pores.

42. The method of any of the claims 37-41 including forming the substrate layer of nitrocellulose or polystyrene.

43. The method of any of the claims 39 or 42, including applying an opaque layer directly or indirectly to the rigid support before applying said substrate layer, for instance
25 by applying a metal oxide layer of sufficient thickness as to be at least partially opaque, to serve as a barrier to transmission of radiation.

44. The method of any of the claims 37-43 adapted for inspecting a substrate-receiving surface, comprising monitoring the electrical condition at one or more test terminals associated with a metal oxide layer lying below said substrate layer while
5 subjecting the substrate layer to conditions by which a defect in said layer produces an electrical change at said terminal, for instance the conditions including subjecting said substrate layer to a corona discharge.

45. The method of any of the claims 37-44 including treating one or more surfaces during the forming of said device by increasing surface energy, or altering the surface structure, or affecting biological binding affinity in the case of a receiving surface for a
10 molecule or bio-material of interest or of a material wished to be rejected, for instance subjecting the surface to corona or flame treatment, or bombardment with ions or sub-atomic particles, or exposure to selected electromagnetic radiation such as gamma radiation or X-rays.

46. The method of any of the claims 37-45 adapted as commercial manufacturing
15 process for production of a support for spotted biological specimens for reaction or analysis and fluorescence measurements for quality assurance, including the step of measuring fluorescence in response to excitation of said support with a wavelength intended to be used with said biological specimen, preferably the process parameters being selected to produce a coating having a fluorescence level of no more than about five times,
20 preferably no more than about three times, or two times the fluorescence obtained from the uncoated rigid member.

47. The method of any of the claims 37-46 for producing a substrate support for spotted biological specimens for reaction or analysis, the steps comprising:

25 (a) at least partially immersing a rigid member that defines a straight support surface (e.g., planar or cylindrical) in a vat containing a coating solution comprising a biologically compatible organic film-forming composition which includes at least one volatile solvent,

(b) progressively drawing the member from the solution along a fixed path into a still environment,

(c) the fixed path being generally parallel to said straight support surface,

(d) the conditions of said still environment enabling said solvent to evaporate to leave a drawn coating of said composition adhered to said support surface, for example the rigid member being a microscope slide, or a component of a bio-cassette of the bottom member of a multiwell plate and the conditions being maintained to cause the formation of a solid film, e.g. a thin film of polystyrene or nitrocellulose, for example the organic film-forming composition comprising nitrocellulose dissolved in amyl acetate or an organic solvent such as acetone, dimethylsulfoxide, ethyl acetate, or other common organic solvents or the organic film-forming composition comprising polystyrene dissolved in an organic solvent such as acetone, dimethylsulfoxide, ethyl acetate, or other common organic solvents, or the method being conducted to produce a micro-porous membrane, such as a nitrocellulose micro-porous membrane, as by dissolving nitrocellulose in methyl acetate, ethyl alcohol, butyl alcohol, water, and glycerol.

48. The method of any of the claims 37-46 including providing said support in the form of a disc having an adherent surface for a substrate coating fluid, spinning said disc individually, preferably the disc being in the form of a compact disc (CD), and providing a substrate coating fluid in the center region of a said disc while it is spinning, to enable radial distribution of said fluid and removal of all except that retainable by action of surface forces.

49. A method of conducting an assay including providing a device according to any of the claims 1-36 or by the methods of claims 37-48, applying an array of spots of bio-material to the substrate, conducting an assay which tags at least some of the spots with a fluorescent label, and, after washing the array, reading the array by fluorescent detection, preferably the assay being based on protein-protein interaction, or involving an array comprising nucleic acid or other genetic material, or comprising viruses, peptides, antibodies, receptors, cDNA clones, DNA probes, oligonucleotides including synthetic

oligonucleotides, or polymerase chain reaction (PCR) products, or the array comprising plant, animal, human, fungal or bacterial cells, or malignant cells, or cells from biopsy tissue.

50. The method of claim 50 wherein the reading is accomplished with a CCD
5 sensor.